REMARKS

By this Amendment, the specification and claims 1 and 24 are amended. Claims 1-63 are pending.

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

The courtesy of Examiners Chunduru and Fredman in granting an interview to Applicants on January 15, 2002 is gratefully acknowledged. Applicants' separate record of the substance of the interview is incorporated into the following remarks.

Attached hereto is a paper, captioned "Amendment Appendix" showing the marked-up version of the changes made by this Amendment.

The specification is amended to correct an obvious typographical error in the cross-reference to one of the parent applications. A Substitute Declaration and Request for Corrected Filing Receipt are also submitted to correctly identify the serial number of the most recently filed parent application.

It is understood from the Office Action and the interview that the objection, the Section 112 rejection and the obviousness rejection of claims 14, 18, 45-46, 59 and 61 over Duck et al. in view of Dervan et al., Pinter et al. and Walder et al. have been withdrawn by the pending Office Action. The remaining rejections are traversed below.

Rejections under 35 U.S.C. § 103(a)

Claims 1-13, 15-17, 19-44, 47-58, 60 and 62-63 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 5,660,988 to Duck et al. in view of U.S. Patent No. 5,874,555 to Dervan et al. Claims 18, 24, 45, 49 and 60-63 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 5,731,146 to Duck et al. in view of U.S. Patent No. 5,403,711 to Walder et al. These rejections are respectfully traversed.

As agreed at the interview, the applied references do not disclose or suggest multiplexes containing Watson-Crick triplets. See the corresponding Interview Summary, which states: "Discussed novel triplex and quadruplex DNA structures comprising Watson-Crick triplets" (emphasis added). Amended claims 1 and 24 specify that at least one of the probe nucleobase sequence and the target nucleobase sequence is double-stranded and is bonded to the other of the probe nucleobase sequence or the target nucleobase sequence solely through Watson-Crick base triplets.

The '988 patent to Duck et al. does not disclose or suggest the use of triplexes or quadruplexes in a catalytic hybridization assay. Rather, the teachings of the '988 patent are confined to duplex hybridization complexes. See, e.g., the '988 patent at column 16, lines 50-67, and the acknowledgment in the Office Action

at line 9 of page 8 that the '988 patent "did not teach formation of multiplex structure."

As discussed in the present specification in the paragraph bridging pages 1-2, Dervan et al. teaches triplexes "based on Hoogsteen binding between limited varieties of adjacent nucleobases, rather than Watson-Crick base pairing." The claimed invention is distinguished from the teachings of references such as Dervan et al., in the following passage from the present specification at page 11, lines 13-17:

> Unlike certain triplexes and quadruplexes discussed in the Background Section above, the preferred multiplex structures of the invention contain at least three strands of nucleic acid bonded together according to traditional Watson-Crick bonding rules.

See also Dervan et al. at column 16, line 67; column 3, line 50 to column 4, line 21; Figs. 9A and 9B; column 13, line 35; column 7, line 31 to column 9, line 24, especially at column 8, lines 39-45.

Thus, the proposed combination of reference teachings fails to meet all the features of the invention of claims 1-13, 15-17, 19-44, 47-58, 60 and 62-63.

The '146 patent to Duck et al. discloses catalytic hybridization assays of single-stranded probes and targets, but states (at column 5, lines 55-58) that assays are not "limited to only situations wherein complementary probe and target sequences

pair to form a duplex." In stating at page 8, line 9 of the Office Action that the '146 patent "did not teach formation of multiplex structure", the Examiner apparently agrees that there is no enabling disclosure in the '146 patent of any hybridization complex other than a duplex. The '146 patent at column 6, lines 9-13, references articles that teach that PNA can be used to form hybridization complexes via a strand invasion mechanism, but such complexes do not contain Watson-Crick triplets.

Walder et al. is likewise acknowledged in the Office Action at page 8, line 12, to teach catalytic hybridization using probe-target duplexes, rather than the multiplexes of the claimed invention. See also Walder et al. at column 3, lines 51-54 and the figures.

Thus, the proposed combination of reference teachings fails to meet all the features of the invention of claims 18, 24, 45, 49 and 60-63.

Accordingly, reconsideration and withdrawal of the obviousness rejections of claims 1-13, 15-45, 47-58 and 60-63 are respectfully requested.

It is noted that claims 14, 46 and 59 are not rejected, and are presumably allowable over the applied references. An indication of such is respectfully requested.

Utility/Enablement

Although the issues of utility and enablement were not raised in the Office Action, Examiner Fredman suggested that Applicants clarify how the application enables a useful and credible invention. Examiner Fredman explained that he tends to look more closely at the level of enablement/credible utility with pioneering inventions exhibiting a high level of novelty, such as the present one.

More specifically, Examiner Fredman explained that he would want to see evidence that the multiplex formed in the claimed invention is not merely an example of strand invasion that has been misinterpreted by the inventors. Accordingly, Applicants enclose a copy of the Rule 132 Declaration of Dr. Jasmine Daksis submitted in the parent application, 09/468,679, which shows that the multiplexes of the invention are not strand-invaded duplexes because: (1) strand invasion is a phenomenon driven by nucleobase-containing sequences having uncharged or partially charged backbones (such as PNA), whereas the overwhelming bulk of Applicants' results relating to mixed sequence triplex formation and all of the quadruplex binding results are obtained from nucleic acids having normally (i.e., completely) charged backbones; and (2) Applicants' data show that increasing salt concentration does not hinder the formation of the multiplexes, whereas strand invasion

decreases with increasing salt concentration due to increased stability of duplexes present.

Also enclosed is a copy of a Rule 132 Declaration by Dr. Richard A. Collins of the University of Toronto, which is being submitted in the parent application. Dr. Collins describes a study confirming the accuracy of Applicants' triplex binding assay, and provides unbiased confirmation of Dr. Daksis' analysis regarding why her assays do not proceed through a strand invasion mechanism.

For at least the reasons set forth above, it is respectfully submitted that the above-identified application is in condition for allowance. Favorable reconsideration and prompt allowance of the claims are respectfully requested.

Should the Examiner believe that anything further is desirable in order to place the application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned attorney at the telephone number listed below.

Respectfully submitted,

CAESAR, RIVISE, BERNSTEIN,
COHEN & POKOTILOW, LTD.

January 23, 2002

By _____

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Please charge or credit our Account No. 03-0075 as necessary to effect entry and/or ensure consideration of this submission.

AMENDMENT APPENDIX
VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

-- This application is a continuation-in-part of U.S. Patent Application No. [09/644,827] 09/664,827, filed September 19, 2000, and a continuation-in-part of U.S. Patent Application Serial No. 09/468,679, filed December 21, 1999, the disclosures of which are incorporated by reference herein in their entireties. --

IN THE CLAIMS:

1. (Amended) A catalytic hybridization composition comprising:

a probe containing at least one probe nucleobase sequence and at least one scissile linkage sequence;

an enzyme adapted to cleave said at least one scissile linkage sequence;

a nucleic acid target containing at least one target nucleobase sequence associated with said nucleobase sequence of said probe by Watson-Crick bonding to form a multiplex structure; and

a hybridization medium containing said probe, said enzyme and said nucleic acid target,

wherein at least one of said probe nucleobase sequence and said target nucleobase sequence is double-stranded and is

bonded to the other of the probe nucleobase sequence or the target nucleobase sequence solely through Watson-Crick base triplets.

24. (Amended) A method for assaying binding, said method comprising:

providing a probe containing at least one probe nucleobase sequence and at least one scissile linkage sequence;

providing an enzyme adapted to cleave said at least one scissile linkage sequence;

providing a target containing at least one target nucleobase sequence;

combining said probe, said enzyme and said target in a hybridization medium further containing water, a buffer and at least one promoter;

incubating said hybridization medium to hybridize said probe nucleobase sequence to said target nucleobase sequence by Watson-Crick bonding to form a multiplex, wherein at least one of said probe nucleobase sequence and said target nucleobase sequence is double-stranded and is bonded to the other of the probe nucleobase sequence or the target nucleobase sequence solely through Watson-Crick base triplets;

cleaving hybridized probes at said at least one scissile linkage to provide unbound probe fragments; and

detecting said unbound probe fragments to assay binding between said probe and said target.